

In the Claims:

Cancel claims 1-4, 6-16, and 18-21, amend claim 5, and add claims 22-48 as follows:

98 5. (Amended) An isolated polypeptide encoded by a purified [the] nucleic acid [of claim 1] comprising a human retinoblastoma gene, or a fragment thereof comprising 15 or more bases.

Sub B1 22. (New) A method of detecting a mutated retinoblastoma ("RB") nucleic acid in mammals, the method comprising the steps of:

- (i) hybridizing an isolated full-length, wild-type RB cDNA probe to a human cell sample; and
- (ii) detecting a mutated RB nucleic acid.

23. (New) A method of detecting a mutated retinoblastoma ("RB") gene in a human, the method comprising the steps of:

- 99
- (i) isolating RNA from a cell sample;
 - (ii) hybridizing the RNA with an isolated full-length, wild-type RB cDNA probe; and
 - (iii) detecting the presence of an abnormal RB RNA, the presence of a normal RB RNA or absence of an RB RNA, wherein the presence of an abnormal RB RNA or the absence of an RB RNA indicates a mutated RB gene.

24. (New) An isolated nucleic acid molecule comprising a nucleotide sequence encoding a full length human wild type retinoblastoma protein, as shown in FIG. 6.

25. (New) The isolated nucleic acid molecule of claim 24, wherein the nucleotide sequence is as shown in FIG. 6.

26. (New) An isolated nucleic acid molecule comprising a nucleotide sequence encoding full-length retinoblastoma protein.

Sub B1 27. (New) The nucleic acid molecule of claim 26, wherein said full-length retinoblastoma protein has the amino acid sequence of exons 1-27, inclusive, as shown in FIG. 6.

28. (New) The nucleic acid molecule of claim 26, wherein said nucleic acid has an open-reading frame, and wherein the 5' end of said open-reading frame is shown at nucleotide position four of the nucleotide sequence shown in FIG. 5, and the 3' end of said open-reading frame is shown at nucleotide position 2784 of the nucleotide sequence shown in FIG. 5.

29. (New) The nucleic acid molecule of claim 26, wherein said retinoblastoma protein is normal retinoblastoma protein.

a9 30. (New) An isolated nucleic acid molecule comprising a nucleotide sequence encoding a retinoblastoma protein, wherein said protein has an amino acid sequence as shown in FIG. 5.

cm 31. (New) A method of using a nucleic acid of any one of claims 24-30 to express a polypeptide encoded by said nucleic acid.

32. (New) An isolated polypeptide encoded by a nucleic acid comprising a human retinoblastoma gene or a fragment thereof, wherein said nucleic acid is selected from the group consisting of:

- (a) a cDNA comprising the sequence of FIG. 5;
- (b) a nucleic acid comprising an exon shown in FIG. 6;
- (c) a nucleic acid that hybridizes specifically under hybridizing conditions to a cDNA comprising the sequence of FIG. 5; and
- (d) a nucleic acid that hybridizes specifically under hybridizing conditions to a cDNA comprising the sequence of FIG. 6.

33. (New) A retinoblastoma polypeptide selected from the group consisting of: (1)

isolated naturally occurring retinoblastoma polypeptide; (2) synthetically produced retinoblastoma polypeptide; (3) retinoblastoma polypeptide produced from purified nucleic acid in an in vitro expression system; (4) retinoblastoma polypeptide encoded by an EcoRI fragment of a retinoblastoma cDNA.

34. (New) The polypeptide of claim 33, wherein said polypeptide is isolated naturally occurring retinoblastoma polypeptide.

35. (New) The polypeptide of claim 33, wherein said polypeptide is synthetically produced retinoblastoma polypeptide.

36. (New) The polypeptide of claim 33, wherein said polypeptide is retinoblastoma polypeptide produced from purified nucleic acid in an in vitro expression system.

37. (New) The polypeptide of claim 33, wherein said polypeptide is encoded by a 3.8 kb EcoRI fragment of a retinoblastoma cDNA.

38. (New) The polypeptide of claim 33, wherein said polypeptide is encoded by a 0.9 kb EcoRI fragment of a retinoblastoma cDNA.

39. (New) A retinoblastoma polypeptide comprising an amino acid sequence encoded by an exon of a retinoblastoma gene, said exon selected from the group consisting of exons 1 to 27, inclusive.

40. (New) The polypeptide of claim 5, wherein said nucleic acid is a cDNA and said cDNA is characterized by the restriction map shown in FIG. 1.

41. (New) The polypeptide of claim 5, wherein said nucleic acid hybridizes specifically under hybridizing conditions to a cDNA comprising the sequence of FIG. 5.

42. (New) The polypeptide of claim 41, wherein said polypeptide is encoded by an allelic variant of said human retinoblastoma gene.